AMENDMENTS TO THE CLAIMS

1.–25. (Canceled)

26. **(Currently Amended)** A method for determining, in a mammal, the susceptibility to a disease associated with β-amyloid formation and/or aggregation ~~such as Alzheimer's disease~~, for determining, in a mammal, the risk of developing a disease associated with β-amyloid formation and/or aggregation ~~such as Alzheimer's disease~~, for screening of the clearance of β-amyloid deposition in a mammal, <u>and</u>/or for predicting the level of β-amyloid burden in a mammal, said method comprising ~~the following steps~~:

   (a) determining, in <u>a first sample obtained from</u> said mammal, the amount of <u>N-terminal truncated and/or post-translationally modified</u> β-amyloid variant ~~according to any of claims 1 to 5~~, the amount of N-terminal APP soluble fragment ~~according to any of claims 6 or 7~~, or the amount of antibody specific for said β-amyloid variant or said APP soluble fragment;

   (b) comparing the amount determined in step (a) with the amount of said <u>N-terminal truncated and/or post-translationally modified</u> β-amyloid variant, ~~said~~ <u>the amount of</u> N-terminal APP soluble fragment, or ~~said~~ <u>the amount of antibody specific for said β-amyloid variant or said APP soluble fragment in a second sample obtained from</u> ~~antibody in~~ a control mammal;

   (c) concluding, from the comparison in step (b), whether the mammal is susceptible to a disease associated with β-amyloid formation and/or aggregation ~~such as Alzheimer's disease~~, whether the mammal is at risk of developing a disease associated with β-amyloid formation and/or aggregation ~~such as Alzheimer's disease~~, whether the β-amyloid deposition in the mammal is cleared, or what the level of β-amyloid burden is in said mammal.

27. (Cancelled)

28. (Cancelled)

29. **(New)** The method of claim 26 comprising:

   (a) determining in the first sample, the amount of N-terminal truncated and/or post-translationally modified β-amyloid variant or the amount of N-terminal APP soluble fragment;

(b)   comparing the amount determined in step (a) with the amount of N-terminal truncated and/or post-translationally modified β-amyloid variant or the amount of N-terminal APP soluble fragment, in the second sample;

(c)   concluding, from the comparison of step (b), whether the mammal is susceptible to a disease associated with β-amyloid formation and/or aggregation, whether the mammal is at risk of developing a disease associated with β-amyloid formation and/or aggregation, whether the β-amyloid deposition in the mammal is cleared, and/or what the level of β-amyloid burden is in the mammal.

30. (New) The method of claim 29 for predicting the level of β-amyloid burden in a mammal, the method comprising:

(a) administering to said mammal a composition for eliciting an immune response or a therapeutic composition comprising an N-terminal truncated and/or post-translational modified Aβ peptide, comprising an antibody that specifically recognizes an N-terminal truncated and/or post-translationally modified Aβ peptide, or comprising a nucleic acid preparation encoding an N-terminal truncated and/or post-translational modified Aβ peptide;

(b) determining in a biological fluid sample obtained from said mammal the amount of N-terminal truncated and/or post-translationally modified β-amyloid variant;

(c) comparing the amount determined in step (b) with the amount of N-terminal truncated and/or post-translationally modified β-amyloid variant in a biological fluid sample obtained from a control mammal;

(d) concluding, from the comparison in step (c) what the level of β-amyloid burden is in said mammal.

31. (New) The method of claim 26 wherein said N-terminal truncated β-amyloid variant starts at position 2, 3, 4, 5, 6, 7, 8, 9, or 10 of β-amyloid.

32. (New) The method of claim 31 wherein said N-terminal truncated β-amyloid variant starts at position 2, 3, 4, 5, 8, 9, or 10 of β-amyloid.

33. (New) The method of claim 32 wherein said N-terminal truncated β-amyloid variant starts at position 3, 4, 5, 8, or 9 of β-amyloid.

34. (New) The method of claim 31 wherein said β-amyloid variant is selected from the group consisting of Aβ(2-42), Aβ(3-42), Aβ(4-42), Aβ(5-42), Aβ(6-42), Aβ(7-42), Aβ(8-42), Aβ(9-42) and Aβ(10-42).

35. (New) The method of claim 26 wherein the post-translationally modified β-amyloid variant is modified by methylation or pyroglutamylation.

36. (New) The method of claim 35 wherein the methylation is present at position 1, 2, 4, or 6 of an N-terminal truncated β-amyloid variant.

37. (New) The method according to claim 35 further characterized in that the pyroglutamylation is present at position 3 of an N-terminal truncated β-amyloid variant starting at position 3 of β-amyloid.

38. (New) The method of claim 26 wherein the C-terminal end of said N-terminal APP soluble fragment consists of position 1, 1 to 2, 1 to 3, 1 to 4, 1 to 5, 1 to 6, 1 to 7, 1 to 8, or 1 to 9 of β-amyloid.

39. (New) The method of claim 26 for determining in a mammal, the susceptibility to a disease associated with β-amyloid formation and/or aggregation, or for determining, in a mammal, the risk of developing a disease associated with β-amyloid formation and/or aggregation comprising:

    (a) determining, in a sample obtained from said mammal: the amount of antibody or reactive T-cells specific for an N-terminal truncated and/or post-translationally modified Aβ peptide; and/or specific for an N-terminal APP soluble fragment, or a C-terminal fragment thereof;

    (b) comparing the amount determined in step (a) with the amount of the antibody or reactive T-cells in a control mammal;

    (c) concluding, from the comparison in step (b), whether the mammal is susceptible to a disease associated with β-amyloid formation and/or aggregation or whether the mammal is at risk of developing a disease associated with β-amyloid formation and/or aggregation;

    wherein an increased amount of antibody or reactive T-cells specific for (i) N-terminal truncated and/or post-translationally modified Aβ peptide; and/or (ii) for N-terminal APP soluble fragment, or for a C-terminal fragment thereof, is an indication that the mammal is susceptible to, or at risk of, developing a disease associated with Aβ formation and/or aggregation.

40. (New) The method of claim 26 wherein at least one of the first and second samples is a brain extract sample or a body fluid sample.

41. (New) The method 40 wherein the body fluid sample is a blood sample or a cerebrospinal fluid (CSF) sample.

42. (New) The method of claim 26 wherein the disease associated with β-amyloid formation and/or aggregation is Alzheimer's disease (AD).

43. (New) The method of claim 26 wherein the susceptibility to Alzheimer's disease (AD) or the risk of developing AD is determined by detecting Aβ(5-42) or Aβ(8-42) in a body fluid sample obtained from the mammal.

44. (New) A diagnostic or theranostic kit comprising one or more of the following:

    (a) a preparation of an N-terminal truncated and/or post-translationally modified Aβ peptide;

    (b) a preparation of an N-terminal APP soluble fragment, or C-terminal fragment thereof; and

    (c) one or more antibodies specifically recognizing an N-terminal truncated and/or post-translationally modified β-amyloid variant; or specifically recognizing an N-terminal APP soluble fragment.

45. (New) The kit of 44 comprising an antibody specifically recognizing an N-terminal truncated and/or post-translationally modified β-amyloid variant and/or an antibody specifically recognizing an N-terminal APP soluble fragment.

46. (New) The kit of claim 45 comprising:

- an antibody (primary antibody) which forms an immunological complex with the N-terminal truncated and/or post-translationally modified Aβ peptide variant or the N-terminal APP soluble fragment to be detected;

- an antibody (secondary antibody) which specifically recognizes the N-terminally truncated and/or post-translationally modified Aβ peptide variant or the N-terminal APP soluble fragment to be detected:

- a marker either for specific tagging or coupling with said secondary antibody;

- appropriate buffer solution for carrying out the immunological reaction between the primary antibody and the N-terminal truncated and/or post-translationally modified Aβ peptide variant or the N-terminal APP soluble fragment, between the secondary antibody and the primary antibody-N-terminal truncated and/or post-transitionally modified Aβ peptide variant or N-terminal APP soluble fragment complex and/or between the bound secondary antibody and the marker; and

- optionally, a purified N-terminal truncated and/or post-translationally modified Aβ peptide or a purified N-terminal APP soluble fragment (or a C-terminal fragment thereof).

47. **(New)** The kit of claim 45 that comprises an antibody that specifically recognizes an N-terminal truncated β-amyloid variant starting at position 5, 6, 8, or 9 of β-amyloid.

48. **(New)** The kit according of claim 45, comprising an antibody that specifically recognizes Aβ(5-42) or Aβ(8-42).

49. **(New)** The kit of claim 45 that comprises a preparation of an N-terminal truncated and/or post-translationally modified Aβ peptide; or a preparation of an N-terminal APP soluble fragment, or a C-terminal fragment thereof.

50. **(New)** A method for the preparation of an antibody that specifically recognizes an N-terminal truncated and/or post-translationally modified β-amyloid variant, the method comprising:
   (a) immunizing an animal with a preparation of an N-terminal truncated and/or post-translationally modified Aβ peptide; or a nucleic acid preparation encoding an N-terminal truncated and/or post-translational modified Aβ peptide;
   (b) obtaining antibodies generated by the immunization in step (a);
   (c) screening the antibodies obtained in step (b) for their specific recognition of N-terminal truncated and/or post-translationally modified β-amyloid variants.

51. **(New)** The method of claim 50 wherein the antibody specifically recognizes an N-terminal truncated β-amyloid variant starting at position 5, 6, 8, or 9 of β-amyloid.

52. **(New)** An antibody obtained by the method of claim 50.

53. **(New)** A method for the preparation of an antibody that specifically recognizes an N-terminal APP soluble fragment, the method comprising:
   (a) immunizing an animal with a preparation of N-terminal APP soluble fragment, or a C-terminal fragment thereof; or with a nucleic acid preparation encoding an N-terminal APP soluble fragment, or a C-terminal fragment thereof;
   (b) obtaining the antibodies generated by the immunization in step (a);
   (c) screening the antibodies obtained in step (b) for their specific recognition of an N-terminal APP soluble fragment.

54. **(New)** An antibody obtained by the method of claim 53.